

REMARKS

Claims 1, 2, and 6-8 are pending in the subject application. Claims 1 and 2 have been amended to more particularly point out what applicants regard as the invention. Support for the amendment to the claims can be found, *inter alia*, for example, page 33 and page 38, lines 24-30. Thus, claims 1, 2, and 6-8 will still be pending and under examination in the subject application upon entry of this Amendment.

In view of the arguments set forth below, applicants maintain that the Examiner's rejections made in the July 21, 2004 Final Office Action have been overcome, and respectfully request that the Examiner reconsider and withdraw same.

The November 2, 2004 Advisory Action

In the November 2, 2004 Advisory Action, the Examiner stated that applicants' October 21, 2004 Amendment would not be entered under 37 C.F.R. 1.121. Applicants maintain that this Preliminary Amendment is in compliance with 37 C.F.R. 1.121, and respectfully requests that it be entered.

Applicants have reiterated their arguments made in their October 21, 2004 Amendment and respectfully request that the Examiner now consider them in this Preliminary Amendment.

Rejection under 35 U.S.C. §112, First Paragraph

The Examiner rejected claims 1, 2, and 6-8 under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. Specifically, the Examiner asserts that references to "the nanomolar range" in

claim 1 and "initially present at a concentration of 1-3 nanomolar" in claim 2 constitute new matter because the concept of each does not appear to be part of the originally filed invention.

In response to the Examiner's rejection, but without conceding the correctness thereof, applicants respectfully point out that claims 1 and 2 have been amended to provide nanomolar amounts supported by the specification, thereby overcoming the objection thereof.

In view of the above remarks, applicants respectfully request that the Examiner withdraw the rejection under 35 U.S.C. §112, first paragraph.

Rejection under 35 U.S.C. §112, Second Paragraph

The Examiner rejected claims 1, 2, and 6-8 under 35 U.S.C. §112, second paragraph, as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the Examiner asserts that references to "the nanomolar range" in claim 1 and "initially present at a concentration of 1-3 nanomolar" in claim 2 render the claims indefinite.

In response to the Examiner's rejection, but without conceding the correctness thereof, applicants again point out that claims 1 and 2 have been amended to more clearly define the metes and bounds of the claimed invention, thereby overcoming the objection thereof.

In view of the above remarks, applicants respectfully request that the Examiner withdraw the rejection under 35 U.S.C. §112, second paragraph.

Rejections Under 35 U.S.C. §103(a)

The Examiner rejected claims 1, 2, 7 and 8 under 35 U.S.C. §103(a) as allegedly unpatentable over Shuman (1992) in view of Bjornson et al. (1994), as evidenced by Stern et al. (1998) and Karn et al. (2001).

In response to the Examiner's rejection, applicants respectfully traverse. Applicants maintain that the cited references fail to support a *prima facie* case of obviousness for the reasons of record and for the additional reasons set forth below.

According to M.P.E.P. §2143, to establish a *prima facie* case of obviousness, the Examiner must demonstrate three criteria with respect to each claim. First, as indicated above, the cited references, when combined, teach or suggest every element of the claim. Second, one of ordinary skill would have been motivated to combine the teachings of the cited references at the time of the invention. And third, there would have been a reasonable expectation that the claimed invention would succeed.

Furthermore, to stress the above points, applicants direct the Examiner's attention to M.P.E.P. §2143.03, which states that "[t]o establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art." *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974). Furthermore, "all words in a claims must be considered in judging the patentability of that claim against the prior art." *In re Wilson*, 424 F.2d 1382, 1385, 165 UPSQ 494, 496 (CCPA 1970). (emphasis added).

In light of these requirements, applicants assert that the cited references fail to support a *prima facie* case of obviousness for claims 1, 2, 7 and 8.

The instant claims provide a method for detecting the release of a single-stranded RNA from an RNA duplex which comprises the steps of (a) admixing an RNA helicase with the RNA duplex under conditions permitting the RNA helicase to unwind the RNA duplex and release single-stranded RNA therefrom, wherein the RNA duplex is (i) present in an amount between 0.1-100 nanomolar and (ii) comprises a first RNA having a first fluorescent label attached at its 5' end and a second RNA having a second label attached at its 3' end, wherein the first fluorescent label produces a luminescent energy pattern when the first RNA is present in the duplex, which differs from the luminescent energy pattern the first RNA produces when it is not present in the RNA duplex; and (b) detecting a change in the luminescent energy pattern produced by the first label so as to thereby detect release of single-stranded RNA from the RNA duplex.

Shuman teaches a method of detection by *gel electrophoresis* of RNA unwinding which uses a *radiolabel* attached to an RNA strand. Shuman fails to teach fluorescently labeled RNA or the detection of nanomolar amounts thereof.

Bjornson teaches a method for detecting the release of a single stranded DNA molecule from a DNA complex. Bjornson fails to teach fluorescently labeled RNA or the detection of nanomolar amounts thereof.

Stern describes in general terms a method utilizing fluorescently labeled RNA. Stern fails to teach the detection

of nanomolar amounts of fluorescently labeled RNA. See e.g., columns 14 and 15, and Figure 5 of Stern.

Karn describes in general terms the fluorescent labeling of an RNA on its 5' or 3' end. Karn does not teach a duplex RNA. Karn fails to teach the detection of nanomolar amounts of fluorescently labeled RNA. Instead, Karn uses nanomolar amounts of labeled RNA to quench the fluorescent signal of a labeled antimicrobial compound. Thus, the labeled RNA is not detected in the method of Karn. Instead, the fluorescence of the labeled antimicrobial compound, and specifically the quenching of that fluorescence, is detected in the method of Karn. See e.g., columns 20-24, and Figures 6-9.

According to M.P.E.P. §2141.02, the claimed invention must be considered as a whole when determining the differences between the prior art and the claims. The Examiner concedes on page 10 of the Office Action that none of the cited references teaches either the detection of nanomolar amounts of fluorescently labeled RNA or a duplex RNA having a different label at the 5' and 3' end of each antiparallel strand in the duplex as taught by the instant claims. However, the Examiner has disregarded these elements of the claimed invention in deciding that the cited references nevertheless render the invention obvious. In the present case, it is clear that the cited references in combination fail to teach each and every element of the claimed invention as a whole because certain elements are not taught by any of the references, i.e. the detection of between 0.1-100 nanomolar of fluorescently labeled RNA or a duplex RNA having a different label at the 5' and 3' end of each antiparallel strand in the duplex. Shuman teaches detection of ssRNA between 20,000,000-50,000,000 nanomolar which is beyond the scope of the claimed invention

while Bjornson teaches detection of nanomolar amounts of DNA only, not RNA. Therefore, one of ordinary skill in the art would not arrive at the subject invention by combining the teachings of the cited references, nor would she be motivated to try.

For the reasons above, the cited references combined fail to teach the elements of the claimed assay. Absent such teaching, there could not have been a motive to combine or a reasonable expectation of success. Therefore, the cited references in combination fail to render obvious the claimed method.

The Examiner also rejected claim 6 under 35 U.S.C. §103(a) over Shuman in view of Bjornson further in view of Nazarenko (1999).

In response, applicants respectfully traverse for the reasons of record and the additional reasons set forth below.

Claim 6 depends from claim 1 and further provides that the first label is fluorescein isothiocyanate and the second label is rhodamine isothiocyanate.

According to the Examiner, Nazarenko teaches an extensive list of suitable moieties that can be used as donor or acceptor molecules for fluorescence resonance energy transfer ("FRET") reactions, including the fluorescein and rhodamine labels recited in claim 6. However, Nazarenko does nothing to overcome the deficiencies of Shuman or Bjornson in failing to teach the detection of nanomolar amounts of fluorescently labeled RNA. Therefore, Nazarenko combined with Shuman and Bjornson, fail to render obvious the claimed method.

The Examiner also rejected claims 1, 2, 7 and 8 under 35 U.S.C. §103(a) as allegedly unpatentable over Eggleston (1996).

In response, applicants respectfully traverse for the reasons of records and the additional reasons set forth below.

Eggleston teaches a helicase assay based upon dye displacement detection methods in which fluorescent dyes which bind to double-stranded DNA are displaced as the DNA is unwound. Eggleston teaches that "since this dye binds to RNA in addition to DNA, it is readily conceivable that RNA helicases may be amenable to this assay if an appropriate ligand...is utilized." (emphasis added). The Examiner states that Eggleston's teachings provide a reasonable expectation of success for practicing the claimed invention.

However, the Examiner appears to have applied an "obvious to try" standard in the present case. It is well settled law that the "obvious to try" standard is not appropriate in the obviousness analysis. See M.P.E.P. §2145. A skilled artisan would recognize that the invention taught by Eggleston is restricted to DNA helicases and that RNA would present obstacles to success that are not present with DNA and for which the claimed invention provides a solution. Specifically, a skilled artisan would recognize that the claimed invention overcomes difficulties not present with DNA, i.e., making an RNA strand and attaching a luminescent dye to it. Even assuming *arguendo* that Eggleston could motivate one to try the claimed invention, it would not present a reasonable expectation of success in doing so. Accordingly, applicants maintain that Eggleston does not render the claimed invention obvious.

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Finally, the Examiner rejected claims 1, 2, 7 and 8 under 35 U.S.C. §103(a) as allegedly unpatentable over Kowalczykowski et al. (1998).

In response, applicants respectfully traverse for the reasons of record and the additional reasons set forth below.

Applicants maintain that Kowalczykowski fails to render obvious the claimed methods for the same reasons as Eggleston fails to do so, namely because the dye displacement assay taught by Kowalczykowski is merely an invitation to try to practice the claimed invention and does not provide a reasonable expectation of success for doing so. Accordingly, Kowalczykowski fails to render the claimed invention obvious.

In view of the above remarks, applicants maintain that the Examiner has failed to set forth a *prima facie* case of obviousness, and that accordingly, claims 1, 2, 7 and 8 satisfy the requirements of 35 U.S.C. §103(a).

Provisional Obviousness-Type Double Patenting Rejection

The Examiner provisionally rejected claims 1, 2, and 6-8 as allegedly unpatentable under the judicially created doctrine of obviousness-type double patenting over claims 1-8 of copending U.S. Application No. 10/182,362. According to the Examiner, a timely filed terminal disclaimer in compliance with 37 C.F.R. §1.321(c) may be used to overcome a provisional rejection based on a nonstatutory double patenting ground.

In response, but without conceding the correctness of the Examiner's rejection, applicants will consider submitting a terminal disclaimer for claims 1, 2, and 6-8 once the rejection is no longer provisional.

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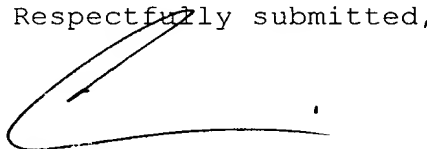
Summary

In view of the remarks made herein, applicants maintain that the claims pending in this application are in condition for allowance. Accordingly, allowance is respectfully requested.

No fee is deemed necessary in connection with the filing of this Amendment. However, if any fee is required, authorization is hereby given to charge the amount of such fee to Deposit Account No. 03-3125.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorneys invite the Examiner to telephone them at the number provided below.

Respectfully submitted,



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